DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-241/S-011
NDA 20-764/S-005

Glaxo Wellcome Inc.
Attention: Elizabeth A. McConnell, Pharm.D.
Project Director, Regulatory Affairs
Five Moore Drive, P.O. Box 13398
Research Triangle Park, NC 27709-3398

Dear Dr. McConnell:

Please refer to your supplemental new drug applications dated August 20, 1999, received November 4, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Lamictal Tablets and Lamictal Chewable Dispersible Tablets.

We acknowledge receipt of your submissions dated October 21, 1999, November 1, 1999, August 28, 2000, and November 27, 2000. Your submission of November 27, 2000 constituted a complete response to our August 24, 2000 action letter.

These supplemental new drug applications provide clinical data in support of a labeling revision to update the Geriatric Use subsection of the Lamictal package insert. Specifically, these applications originally proposed to include standard language contained in paragraph (B) under 21 CFR 201.57(f)(10)(ii), which basically states that no differences in safety or effectiveness have been observed between elderly and younger subjects. Currently, as amended, these applications propose revised standard language (as recommended in the Agency's August 24, 2000 action letter) contained in paragraph (A) under 21 CFR 201.57(f)(10)(ii), which basically states that dose selection in the elderly should be cautious.

We have completed the review of these supplemental applications, as amended, and have concluded that adequate information has been presented to demonstrate that the drug products are safe and effective for use as recommended in the agreed upon labeling text. Accordingly, these supplemental applications are approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed draft labeling text (dated May 25, 2001), and must be formatted in accordance with the requirements of 21 CFR 201.66. Marketing the products with FPL that is not identical to the approved labeling text and "Drug Facts" format may render the products misbranded and unapproved new drugs.

Please submit the copies of final printed labeling (FPL) electronically to each application according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*

(January 1999). Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Please individually mount ten of the copies on heavyweight paper or similar material. For administrative purposes, these submissions should be designated "FPL for approved supplements NDA 20-241/S-011 and 20-764/S-005." Approval of these submissions by FDA is not required before the labeling is used.

In addition, we note that your November 27, 2000 response to our August 24, 2000 action letter did not include new data or new analyses. We remind you that our action letter requested that you further evaluate any potential differences between the pharmacokinetics in the elderly and younger adults. Specifically, based on our initial review of these applications, there is a suggestion of a 33% difference in clearance between elderly and young adults in one comparison of the 2 groups, the UK study in 12 elderly and 12 younger adults. While the clearance in these 12 elderly patients is comparable to the clearance in an extended sample of young adults, we believe the discrepancy in the UK study requires explanation. Therefore, we are asking you, again, to revisit this issue and explore explanations for these results. As we stated in our action, we would be happy to discuss this with you, but at the least we ask you to submit a discussion of these discrepant results.

Lastly, please submit three copies of the introductory promotional materials that you propose to use for these products. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional materials and the package inserts directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Jacqueline H. Ware, Pharm.D., Regulatory Management Officer, at (301) 594-5533.

Sincerely,

{See appended electronic signature page}

Russell Katz, M.D.
Director
Division of Neuropharmacological Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research